Application No. 10/078,757 - - - - - 2

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (currently amended). A method of producing a humanized mouse monoclonal antibody which consists of the steps:

(a) constructing a first human antibody heavy or light chain library consisting of antibody heavy chains or antibody light chains in which each chain in the first human antibody light or heavy chain library has three complementarity determining region (CDR) loops ~~and at least one such loop is flanked by unaltered human framework residues and has the amino acid sequence of a corresponding mouse antibody heavy or light chain CDR loop~~ in which the complementarity determining region three (CDR3) loop in each light or heavy chain has the amino acid sequence of a corresponding mouse antibody heavy or light chain CDR3 loop and is flanked by unaltered human framework residues;

(b) constructing a second human antibody heavy or light chain library consisting of antibody heavy chains or antibody light chains, in which each chain in the second human antibody heavy or light chain library has three complementarity determining region (CDR) loops ~~and at least one such loop is flanked by unaltered human framework residues and has the amino acid sequence of a corresponding mouse antibody heavy or light chain CDR loop;~~ in which the complementarity determining region three (CDR3) loop in each light or heavy chain has the amino acid sequence of a corresponding mouse antibody heavy or light chain CDR3 loop and is flanked by unaltered human framework residues; wherein the chains of said second human antibody heavy or light chain library are the complementary heavy or light chain of said first human antibody heavy or light chain library chains, such that one library is a light chain library and the other library is a heavy chain library;

(c) creating a library of heavy and light chain pairs by combining chains from said first human antibody heavy or light chain library of step (a) with a complementary chain

Application No. 10/078,757 - - - - - 3

from an antibody which binds a preselected antigen forming a library of heavy and light chain pairs;

     (d) isolating antigen binding chains of step (a) by selecting from the library of step (c), a heavy and light chain pair which binds to said preselected antigen, isolating from the antigen binding heavy and light chain pair, the antigen binding chains of step (a);

     (e) creating a humanized pair library by combining isolated antigen binding chains of step (d), with chains of said library of step (b), so that a first isolated chain of step (d), together with a complementary second chain in said library of step (b) combine to form a heavy and light chain humanized pair library;

     (f) selecting from the humanized pair library of step (e) a humanized heavy and light chain pair that binds to said preselected antigen; and

     (g) combining two of said selected humanized heavy and light chain pair of step (f) to form a ~~whole antibody~~ whole antibody; wherein said humanized mouse monoclonal antibody binds the same antigen as the mouse monoclonal antibody.

Claim 2 (previously presented). The method of claim 1 wherein the first human antibody heavy or light chain library contains only light chains and the complementary chain is a heavy chain.

Claim 3 (previously presented). The method of claim 1 wherein the first human antibody heavy or light chain library contains only heavy chains and the complementary chain is a light chain.

Claim 4 (original). The method of claim 1 wherein the heavy chain is a Fd fragment.

Claim 5 (currently amended). A method of producing a humanized mouse monoclonal antibody heavy and light chain pair which consists of the steps:

     (a) constructing a human light chain library wherein each light chain of said light chain library has three complementarity determining region (CDR) loops, ~~at least one of said CDR loops having an amino acid sequence corresponding to that of a mouse light chain CDR loop and is flanked by unaltered human framework residues~~ in which the complementarity determining region three (CDR3) loop in each light chain has the amino acid sequence of a corresponding mouse antibody light chain CDR3 loop and is flanked by unaltered human framework residues;

Application No. 10/078,757 - - - - - 4

(b) selecting a light chain from the light chain library of step (a), wherein the selection comprises combining a heavy chain from an antibody that binds a preselected antigen with a light chain from the library of step (a) to form a heavy and light chain pair library, screening said pair library for binding to said preselected antigen, and isolating light chains that bind to said preselected antigen;

(c) constructing a library of human heavy chains wherein each heavy chain of said library of human heavy chains has three CDR loops, ~~at least one of said CDR loops having an amino acid sequence corresponding to a mouse heavy chain CDR loop and is flanked by unaltered human framework residues~~ in which the complementarity determining region three (CDR3) loop in each heavy chain has the amino acid sequence of a corresponding mouse antibody heavy chain CDR3 loop and is flanked by unaltered human framework residues;

(d) combining a heavy chain from the heavy chain library of step (c) with a selected light chain of step (b) to produce a second library of humanized mouse monoclonal antibody heavy and light chain pairs;

(e) isolating an antigen binding humanized mouse monoclonal antibody heavy and light chain pair from the library of step (d) by screening said library of step (d) for binding with said preselected antigen and isolating those humanized mouse monoclonal antibody heavy and light chain pairs that bind said ~~preselected antigen~~ _preselected antigen; wherein said preselected antigen is the same antigen recognized by the mouse monoclonal antibody._

Claim 6 (previously presented): The method of claim 5 further comprising converting the selected heavy and light chain pair to a whole antibody.

Claim 7 (original). The method of claim 5 wherein the heavy chain of step (b) is a Fd fragment.

Claim 8 (original). The method of claim 7 wherein the heavy chain Fd is a humanized mouse heavy chain fragment or a template mouse heavy chain fragment.

~~Claim 9 (cancelled).~~

~~Claim 10 (cancelled).~~

Claim 9 11 (original). The method of claim 5 wherein in step (b) a humanized mouse heavy chain is used.

Application No. 10/078,757 - - - - - 5

Claim 12 [10] (currently amended). The method of claim 5 wherein ~~only a light chain complementarity~~ the CDR3 loop in each light and heavy chain is a CDR3 loop from antibody LM609 produced from hybridoma cell line deposited with American Type Culture Collection under ATCC Accession No. HB 9537 ~~is grafted in place of the LCDR3 loop of a light chain of step (a)~~.

~~Claim 13 (cancelled).~~

Claim 14 [11] (original). The method of claim 7 wherein the heavy chain Fd is a humanized mouse heavy chain.

Claim 15 [12] (original). The method of claim 7 wherein the heavy chain Fd is a template mouse heavy chain fragment.